valves switching.

2. The fluid pumping system of claim 1 wherein said the piston stroke length is adjustable and the piston refill stroke start and stop for the given length is in synchronization with switching valve open and close to solvent reservoir.
3. The fluid pumping system of claim 1 contains a Servomotor, a gear motor, a stepping motor, or a combination of motors and gearboxes with an optical encoder.
4. The fluid pumping system of claim 1 wherein said the pump can be operated as a syringe pump or a reciprocating pump by using a closed loop digital controlled by a computer software or firmware operation system.
5. The fluid pumping system of claim 1 contains a flex coupler to connect the motor to a Linear Actuator to facilitate linear driving of a piston that is mounted securely to the piston holder mounted on the actuators moving plate form.
6. A method of proportioning fluid to form a fluid composition or flow gradient, comprising the steps of:
   Providing a plurality of pumps each connected to a respective fluid from a corresponding one of a plurality of reservoirs or each connected to a plurality of reservoirs;
   Providing a plurality of switching valves each connected to a column or columns for on-line fluidic switching;
   Providing a plurality of separation columns to facilitate a separation of complex sample or samples based on a combination of more than two of the following separation methods: reversed phase, normal phase, ion exchange, size exclusion, affinity chromatography, gel permeation chromatography, electrical field assisted PH gradient , chiral chromatography, metal chelating or affinity, isotope labeling tag, super-critical fluid chromatography, high temperature liquid chromatography, capillary electrophoresis(CE), capillary electro-chromatography(CEC), displacement chromatography, perfusion chromatography, and

turbulence flow chromatography;

A gradient proportioning pumping system for on-line fully automated separation of proteins or the reaction products of proteins. An example based on the Isotope-Coded Affinity Tag (ICAT™) chemistry as presented by Goodlett et al (U.S. patent number: 6,629,040), or based on IMAC (Immobilized metal affinity chromatography (IMAC) (L. Anderson et al Anal biochem. 1986, 154(10), 250-254), comprising:

A multi-channel pumping system including Six to eight pumps for a plurality of solvents; a strong cation exchange column, a reversed phase trapping column, an affinity column (Avidin affinity column), a cleavage column or multiple of cleavage columns, a nano-trap column, an analysis nano-LC column, a Mass Spectrometer, an auto-sampler, an injection valve or switching valve, three to four additional flow path diverting valves, one to two Tees, a spray tip or a nano-column with spray tip for Mass Spectrometer, and the Reagents prescribed in the Applied Biosystems ICAT™ kit (Applied Biosystems ICAT™ Cleavable ICAT™ Reagent Methods Development Kit, Part number 4339035).

7. The switching valve of the claim 6 includes also a multiple channel selection valves for on-line multiple sample parallel cleavage operations or sample collections
8. The auto-sampler injection valve of the claim 6 includes also a manual or time programmable injection valve;

9. A method for on-line automated ICAT™ protein or protein reaction products separation, identification, and quantification comprising

Step 1: Sample injection into an ion exchange (SCX) column

Step 2: By controlling composition ratio of elution strength of solvent, the sample trapped in the ion exchange column can be either partially eluted in a controlled fraction or completely eluted from the ion exchange column.

Step 3: for removing salt and to condition the trapping column to PH =7.2

step 4: for conditioning the Avidin column to PH =7.2.

step 5: for neutralizing the ion exchange and Avidin columns after sample loading.

step 6: for removing non-Biotin labeled peptides

step 7: for eluting labeled cystein containing peptides from the Avidin column into the cleavage column. A 10-port or more than 10 port selection valve is used for switching the flow paths to a array of collection vials, plates, or cleavage columns for further processing.

step 8: for pumping the cleavage reagent A and B that is freshly prepared by the auto-sampler into the cleavage column at 37°C for Biotin cleavage of the cystein containing peptides.

step 9: for connecting the cleavage column, an electrode, and a pre-column to the first Tee or cross. The pre-column is then connected to a second Tee where the analysis nano-LC column and a waste solvent transfer line are also connected. The outlet of the solvent waste transfer line is connected to a 6 port or a 4 port-switching valve for flow stream diversion. In this particular arrangement peptides of interest are trapped and concentrated at the pre-column and sample solvent goes to waste.

step 10. Wherein the sample is chromatographically separated using nano-LC or capillary-LC binary gradient in both the pre-column and the analysis nano-LC column and then is sprayed into mass spectrometer ionization source for identification and quantification. The nano-LC fluid pumping system of claim 1 in splitless mode at 0.1 to 1.0 µl/min flow rates is a particularly useful because of its nano-flow gradient capability.

Step 11: allows the sample in the ion exchange column is again eluted into the trap column to repeat those steps 1

through 10 again until the whole peptide sample in the ion exchange column has been completely eluted and analyzed;

10. A gradient proportioning pumping system of claim 6 for on-line fully automated separation of proteins or protein reaction products in proteome analysis, carbohydrates analysis, phosphoprotein isotope-coded affinity tag chemistry (M. B. Goshe et al, Anal Chem. 2001, 73, 2578-2586), Immobilized metal affinity chromatography (IMAC) (L. Andersson et al Anal biochem. 1986, 154(10), 250-254), and Multidimensional protein identification technology (MudPIT)(A.J.Link et al Nat. Biotechnol. 1999, 17, 676, W. H. McDonold et al Intern. J. Mass Spec 2002, 219, 245-251), capillary eletrophoresis, or other technology where multiple high pressure fluid delivery and valve switching, nano-flow rates, micro-flow rates, and analytical flow rates fluid delivery are necessary.

Abstract:

A fluid pumping system can be operated in dual control modes: as a syringe pump for nano-flow solvent delivery; and as a reciprocating pump for micro- and analytical flow solvent delivery. The fluid pumping system is also operated in a closed-loop digital control process using an optical encoder for piston